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ORAL SNUFF, SMOKING HABITS AND ALCOHOL CONSUMPTION IN RELATION TO ORAL CANCER IN A SWEDISH CASE-CONTROL STUDY

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The use of oral snuff is a widespread habit in Sweden. We investigated whether the use of Swedish moist snuff leads to an increasing risk of oral cancer. Other risk factors such as smoking tobacco and alcoholic beverages were also investigated. Our study comprised 410 patients with oral cancer, from the period 1980–1989, and 410 matched controls. All subjects received a mailed questionnaire. The response rates were 96% and 91% for cases and controls, respectively. In the study, a total of 20% of all subjects, cases and controls, were active or ex-snuff users. The univariate analysis did not show any increased risk [odds ratio (OR) 0.7, 95% confidence interval (CI) 0.4–1.1] for active snuff users. We found an increased risk (OR 1.8, CI 1.1–2.7) for oral cancer among active smokers. Alcohol consumption showed the strongest risk for oral cancer. Among consumers of beer, an increased risk of 1.9 (CI 0.9–3.9) was found. Corresponding ORs for wine and liquor were 1.3 (CI 0.9–1.8) and 1.6 (CI 1.1–2.3), respectively. A dose-response effect was observed. Although not statistically significant, a multivariate analysis similarly suggested that the most important risk factors were beer and liquor consumption, followed by smoking. *Int. J. Cancer* 77:341–346, 1998.
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Oral cancer is a disease with an increasing incidence and a rising mortality in most West European countries. In males, it is most common in France and India. High rates are also reported from countries in Central Europe, including Switzerland, Slovakia, Slovenia and Hungary. Consistently low rates are reported from Japan, China and countries of Northern Europe. For women, high rates are found in India, countries of Southeast Asia and the United States (Boyle *et al.*, 1995).

During the 1950s, 1960s and 1970s, epidemiological reports noted continuing decreases in the incidence of intraoral cancer, *e.g.*, in the United States, Australia and countries of Western, Central and Eastern Europe (Boyle *et al.*, 1995). Data for more recent time periods, however, suggest that oral cancer is now increasing. A low rate is still reported from Scandinavia, but slowly increasing incidence rates among men even in Sweden and Norway have been reported (Hakulinen *et al.*, 1986). In Sweden, intraoral cancer accounted in 1993 for 1.5% and 0.8% of all malignant tumors among Swedish men and women, respectively (National Board of Health and Welfare, 1992). In Denmark, there has been a steep rise in incidence during the past decades (Hakulinen *et al.*, 1986; Bundgaard *et al.*, 1995). On the other hand, no increase in the incidence for oral cancer has been reported in Finland (Hakulinen *et al.*, 1986).

The relationship between tobacco smoking and alcoholic beverages and oral cancer has been described repeatedly (Bundgaard *et al.*, 1995; Blot *et al.*, 1988; Mashberg *et al.*, 1993; Franceschi *et al.*, 1992). These factors are the 2 strongest individual risk indicators for oral cancer known at present. Regarding some types of smokeless tobacco, *e.g.*, moist snuff, no relation with oral cancer has been established.

Ahlbom (1937) has observed that Swedish patients with buccal, gingival or "mandibular" cancer reported the use of snuff or chewing tobacco more frequently than patients with other types of cancer. Case reports of oral cancer among users of snuff or chewing tobacco also appeared in the United States (Wynder *et al.*, 1957*a*). The first modern epidemiological study concerning smokeless tobacco was conducted by Wynder *et al.* (1957*b*) and indicated an increased risk of buccal and gum cancer in snuff users. Concurrently with the investigation presented here, another Swedish epidemiological study has been performed by Lewin *et al.* (1998), who investigated the role of Swedish snuff for cancer of the oral cavity, pharynx, larynx and esophagus. The results could not confirm any association between cancer and the use of oral snuff.

There are 2 main types of snuff: moist and dry. Moist snuff is mainly used in Scandinavia and the United States, and it is usually kept in the gingival-buccal area. The Swedish moist snuff is a non-fermented variety. The ground tobacco, after addition of salt and water, undergoes a heath treatment which renders it practically free from microorganisms, lowering the risk of nitrate formation and subsequent formation of nitrosamines.

In United States, the moist snuff is a fermented product. The fermentation is a spontaneously occurring biochemical process in the moistened tobacco which causes chemical changes (IARC, 1985).

In Sweden, the use of oral snuff has been a traditional and well-established habit for several decades. Due to concerns about health hazards, it has been vigorously debated within Sweden, especially during the last few years.

The most common snuff type in Sweden is loose moist snuff used as a 1–2 g quid, which is formed by the fingers and generally placed under the upper lip. A portion-bag-packed snuff is now often used, which consists of a 0.5 or 1 g portion of moist snuff. By far, Sweden has the highest *per capita* sales figures in the world for moist snuff. In 1989, 4,850 tons were sold, *i.e.*, 0.6 kg *per capita* (Andersson, 1991), and in 1995 the sale had increased to 5,400 tons.

In our study, the risk for oral cancer was evaluated in relation to exposure to moist snuff, smoking and alcohol. In another report, based on the same material, we shall present the risk for oral cancer according to other factors, *e.g.*, oral infections, dental status, anemias, occupations and occupational exposures.

MATERIAL AND METHODS

Our population-based case-control study included all histopathologically verified squamous cell oral cancer cases (ICD-7 codes 140, 141, 143–145) diagnosed in the 4 most northern counties in Sweden—Norrbotten, Västerbotten, Jämtland and Västernorrland—during 1980–1989 and reported to the Cancer Registry.

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Cases

Of 419 identified patients, 1 was excluded because of wrong diagnosis coding and 8 deceased cases due to lack of relatives. Thus, our study comprised in total 410 cases, distributed as described in Table I. The mean age was 72.3 years for women and 69.6 years for men.

Controls

For each of the 175 living cases, 1 living control was drawn from the National Population Registry. The person closest in age, *i.e.*, with the closest personal identification number, with the same sex and living in the same county, was used. For each of the 235 deceased cases 1 deceased control was selected from the National Registry for Causes of Death. The same matching criteria were used (age, sex, county) and furthermore, deceased controls were matched on year of death.

Assessment of exposure

All of the 350 living subjects received a mailed questionnaire. To obtain information concerning deceased persons, the questionnaire was sent to the next-of-kin defined in the order of husband or wife, child, parent, sibling or other. The specific nature of the investigation was not disclosed, and there was no reference to the disease under study. Instead, the general information given was that different factors of potential importance for health were studied. The questions concerned different exposure factors of possible importance for oral cancer. This report deals with exposure to tobacco and alcoholic beverages, and the following factors were taken into account.

Tobacco exposure. Use of moist snuff, cigarettes, cheroots, cigars and pipe tobacco was covered. The questionnaire mapped both the daily consumption and the time period of smoking. In the analysis, lifetime consumption (kg tobacco) was assessed. All tobacco exposure was expressed in grams of tobacco/day. One cigarette is equivalent to 1 g of tobacco, 1 cheroot to 3 g and 1 cigar to 5 g. One pack of pipe tobacco is equivalent to 50 g of tobacco and 1 pack of moist snuff to 50 g. One quid of moist snuff is estimated to contain 1 g of tobacco. The brand of snuff was also recorded.

An ex-smoker or ex-snuff user was defined as a person who had quit the habit at least 1 year before the diagnosis; for controls, the corresponding year was the year of diagnosis for the respective case. Subjects who had stopped smoking or stopped using moist snuff within the year before diagnosis were coded as current users of tobacco and with a daily consumption corresponding to the actual consumption by the time they quit.

Alcohol exposure. These questions covered the use of light beer (alcohol content less than 4.5 volume %), beer (alcohol content minimum 4.5 volume %), wine and liquor. The questionnaire asked for weekly consumption and if there was any substantial change over the years.

The subjects were asked to estimate the light beer consumption according to 4 alternatives: (1) no light beer at all; (2) 1–9 light beer bottles (33 cl)/week; (3) 10–19 bottles/week; (4) at least 20 bottles/week. Beer consumption was surveyed in a corresponding way with the following 4 alternatives: (1) no beer at all; (2) 1–4 beer bottles/week; (3) 5–9 bottles/week; (4) at least 10 bottles/week.

Estimation of wine and liquor exposure was made with regard both to how often the subjects drank and to the average amount each time. Regarding the frequency of wine drinking, the subjects had to choose between 5 alternatives: (1) never; (2) seldom; (3) about once a month; (4) about once a week; (5) daily. As for the approximate quantity on each occasion, there were 3 alternatives: (1) not more than 1 glass; (2) about 2 glasses; (3) 1 bottle or more. The results of these answers were transformed into a score taking amount and frequency into account. The different categories are described in the Results.

For liquor consumption, the same frequency alternatives were used as for wine, but regarding the quantity per occasion 4 alternatives were given: (1) not more than 1 glass; (2) about 2 glasses; (3) about 37 cl; (4) more than 37 cl. The answers regarding liquor consumption were also transformed into an exposure score.

If the questionnaire was incomplete or a question was obviously misunderstood, the subject was contacted by telephone by a specially trained interviewer who did not know whether the person under investigation was a case or a control, and the data were supplemented according to written instructions. Five persons were unable or unwilling to answer the questionnaire, but accepted a full telephone interview.

After the questionnaire had been completed by the interviewer, the front page including name, personal identification number and address was removed, thus enabling a blind coding of the answers.

Statistical methods

In the univariate and the multivariate analyses, conditional logistic regression was used with 708 subjects and 354 numbers of matched pairs. The calculations were performed using the EGRET program (Epidemiological Graphics Estimation and Testing package, SERC, Seattle, WA). The variables were expressed in categorical forms and the results are presented as the odds ratio (OR) and 95% confidence interval (CI) in the particular category compared with the reference category.

TABLE I – NUMBER OF THE INTERVIEWED FEMALES AND MALES, CASES AND CONTROLS, BEFORE AND AFTER EXCLUDING OF INCOMPLETE PAIRS

	Initially included	Females	Males	Refusers	Remaining after exclusion	Females	Males
Cases	410	134	276	18	354	117	237
Alive	175	53	122	11	143	43	100
Deceased	235	81	154	7	211	74	137
Controls	410	134	276	38	354	117	237
Alive	175	53	122	21	143	43	100
Deceased	235	81	154	17	211	74	137

RESULTS

Of 410 cases, 11 living subjects and 7 next-of-kins to deceased persons refused to participate. Corresponding numbers of refusers for controls were 21 alive subjects and 17 next-of-kins to deceased persons. This gave a response rate of 96% and 91% for cases and controls, respectively. Since we used a matched study design, the 56 refusers and their counterparts were excluded from further analysis, which thus deals with the remaining 708 subjects or 354 matched pairs distributed as described in Table I.

Univariate analyses

Snuff. Of the 708 subjects in this study, 20% were active or ex-snuff users, 67 cases and 72 controls. Only 1 woman reported use of moist snuff. The univariate analysis yielded for active snuff users OR 0.7 (CI 0.4–1.1) and for ex-users of snuff OR 1.5 (CI 0.8–2.9) (Table II). When analyzing only the alive snuff users, the OR for active use decreased to 0.5 (CI 0.2–1.2) and increased for ex-use to 3.0 (CI 0.9–9.4).

When snuff users, active and ex-users, were analyzed according to whether they had smoked or not, increased risks were observed for ex-snuff users regardless of smoking habits, but only significantly increased if the subjects also were active smokers (OR 3.1, CI 1.4–6.8) (Table III). On the other hand, active snuff users did not experience any significantly increased risk regardless of smoking habits (Table III).

To investigate whether a dose-response effect pertained, we divided the snuff users into 2 groups according to lifetime consumption if we were able to assess duration of use. The median value among the controls in kg was calculated to 156.0 kg, which corresponds to about 2 packages (100 g) of snuff per day during

TABLE II – ORs AND 95% CIs FOR THE DIFFERENT VARIABLES CONCERNING TOBACCO AND ALCOHOL CONSUMPTION. UNIVARIATE ANALYSIS

Exposure factors	Ca/Co[1]	OR	95% CI
Oral snuff			
Never snuff user	287/282	1.0	—
Active	39/54	0.7	0.4–1.1
Ex-user	28/18	1.5	0.8–2.9
Ever user	67/72	0.9	0.6–1.4
Smoking			
Never smoker	152/171	1.0	—
Active	122/88	1.8	1.1–2.7
Ex-smoker	80/95	1.0	0.6–1.6
Ever smoker	202/183	1.3	0.9–1.9
Chewing tobacco	5/8	0.6	0.2–2.0
Light beer	148/120	1.4	1.0–2.0
Beer	27/16	1.9	0.9–3.9
Wine	188/168	1.3	0.9–1.8
Liquor	234/202	1.6	1.1–2.3

[1]Ca/Co = cases/controls.

TABLE III – ORs FOR NON-USERS, EX-USERS AND ACTIVE USERS OF SNUFF IN RELATION TO SMOKING HABIT

Snuff use	*Smoking*	*Ca/Co*[1]	*OR*	*95% CI*
Never snuff user	Never smoker	124/144	1.0	
	Ex-smoker	54/67	0.9	0.6–1.4
	Active smoker	109/71	1.7	1.1–2.6
Ex-user of snuff	Never smoker	9/4	1.8	0.9–3.5
	Ex-smoker	16/13	1.6	0.8–3.4
	Active smoker	3/1	3.1	1.4–6.8
Active snuff user	Never smoker	19/23	0.7	0.4–1.2
	Ex-smoker	15/10	0.6	0.3–1.3
	Active smoker	10/16	1.2	0.6–2.4

[1]Ca/Co = cases/controls.

roughly 30 years. Life consumption over 156.0 kg yielded OR 1.1 (CI 0.5–2.0); less than that, OR 0.8 (CI 0.4–1.5).

The most common tumor site in this material was the lip. When analyzed separately, an increased risk was found for lip cancer (OR 1.8, CI 0.9–3.7) among ex-snuff users. The risk was close to unity for current users. For all other sites combined, a decreased risk was found for active users of snuff with OR 0.4 (CI 0.1–0.9).

No difference in risk was found among the different snuff brands used.

Smoking. Of the subjects in the study, 30% were active smokers and 25% were ex-smokers. Among the cases, 34% were active smokers and 23% ex-smokers. Corresponding numbers among controls were 25% and 27%, respectively. In the group of active or ex-smokers, 76% used cigarettes, 55% used pipe and only 5% used cigars or cheroots.

The univariate analysis showed a statistically significant increased risk for developing oral cancer among active smokers (OR 1.8, CI 1.1–2.7), whereas no increased risk was found for ex-smokers (Table II). A division of ex-smokers into 2 groups according to whether they had stopped smoking for more or less than 10 years, did not yield any increased risk either (data not shown). When analyzing only the alive smokers, the OR for active smoking decreased to 1.7 (CI 0.8–3.3). For ex-smoking, the result did not change.

To investigate whether there was a dose-response effect in the group who could state their extent of consumption, we divided tobacco smokers into 2 groups according to lifetime consumption. The median value among the controls was calculated to 124.8 kg, which corresponds to about 1 package of cigarettes per day during 17 years. Current smokers with >124.8 kg lifetime consumption of tobacco had a significantly increased risk for oral cancer (OR 1.8, CI 1.2–2.8). Lower consumption produced a risk around unity.

When dividing the material according to localization, an increased risk was found among smokers for cancer in the floor of the mouth (OR 8.0, CI 1.0–64.0).

Pipe smokers were also analyzed separately, first regardless of localization, then divided into two groups; lip and other sites. The analysis for all localizations together showed a non-significant OR of 1.2 (CI 0.7–1.9) among ever pipe smokers. The group of pipe smokers was also divided into current and ex-smokers. Among current pipe smokers, significantly increased ORs were produced for all localizations together (OR 2.0, CI 1.1–3.4) and all localizations combined excluding lip (OR 3.1, CI 1.3–7.5), whereas no significantly increased risk was found for lip cancer (OR 1.5, CI 0.7–3.1).

Chewing tobacco. Only 13 individuals (5 cases and 8 controls) were, or had regularly been, users of chewing tobacco (OR 0.6, CI 0.2–2.0) (Table II).

Alcohol. Except for active smoking, some types of alcohol showed the strongest association with oral cancer in this study, as shown in Table II.

Light beer: Our results showed an increased risk for oral cancer among consumers of light beer (OR 1.4, CI 1.0–2.0) (Table II). This risk was particularly strong among those who consumed 10–19 bottles/week (OR 9.7, CI 2.2–43) based on 18 cases and 3 controls. A consumption of ≥20 bottles/week gave a possibly less pronounced increased risk of 4.8 (CI 1.0–23) based on 9 cases and 2 controls.

Beer: An increased risk for oral cancer was found among consumers of beer (OR 1.9, CI 0.9–3.9) (Table II). The individuals who reported beer drinking were divided into 2 groups: one group (22 cases and 13 controls) consumed 1–4 bottles/week and the other group (5 cases and 3 controls) consumed at least 5 bottles/week. In both groups, an increased risk for oral cancer was calculated, with an OR of 1.8 (CI 0.4–7.7) in the high group and an OR of 1.9 (CI 0.8–3.9) in the low group.

Wine: Of the 708 subjects in the study, 356 reported wine drinking. Wine consumption in general did not show a statistically significant increased risk for oral cancer (OR 1.3, CI 0.9–1.8) (Table II). Using a score system taking amount and frequency into account, high consumption gave an OR of 8.6 (CI 1.0–70) (Table IV).

Liquor: Liquor consumption showed an increased risk for oral cancer (OR 1.6, CI 1.1–2.3) (Table II). Among the responders, more than 50% belonged to the group of low consumers. Using the same score system as for wine, significantly increased risks for oral cancer were found among medium and high consumers of liquor (Table IV). The individuals in the medium group showed an OR of 1.6 (CI 1.0–2.7) and those with the highest consumption yielded an OR of 3.6 (CI 1.8–7.2). When analyzing only alive individuals reporting liquor consumption, the OR decreased to 1.1 (CI 0.6–1.8).

The score system described for wine and liquor does not correspond exactly to the amount of beverages consumed. Thus, persons who have consumed relatively small amounts daily tend to accumulate larger amounts during lifetime than those who drink much and seldom. It is unclear whether the frequency of drinking or the total amount consumed is of greatest importance in carcinogenesis. We have also analyzed the total volume consumed without considering the frequency of consumption. In this analysis, we found a similar dose-response effect as in the score analyses (Table IV).

Multivariate analyses

The multivariate analysis is based on ever habits according to snuff use, smoking and alcohol. The most important risk factors

TABLE IV – WINE AND LIQUOR SCORES BASED ON DRINKING HABITS[1]

Amount of wine	Amount of liquor	Rarely	Approx. once a month	Approx. once a week	Daily
≤1 glass	≤1 glass (6 cl)	1	2	3	4
Approx. 2 glasses	Approx. 2 glasses	2	4	6	8
Approx. 75 cl	Approx. 37 cl	3	6	9	12
>75 cl	>37 cl	4	8	12	16
			Ca/Co[2]	OR	95% CI
Wine group	1 = score 1–3		150/132	1.3	0.9–1.8
Wine group	2 = score 4–8		25/32	0.9	0.5–1.8
Wine group	3 = score 9–16		8/1	8.6	1.0–70
Liquor group	1 = score 1–3		125/125	1.3	0.9–2.0
Liquor group	2 = score 4–8		60/53	1.6	1.0–2.7
Liquor group	3 = score 9–16		42/18	3.6	1.8–7.2
Wine group	1 = <75 cl		166/149	1.3	0.9–1.8
Wine group	2 = 75–300 cl		12/14	1.0	0.4–2.4
Wine group	3 = >300 cl		5/2	2.7	0.5–15
Liquor group	1 = <37 cl		152/152	1.4	0.9–2.0
Liquor group	2 = 37–148 cl		47/35	2.0	1.1–3.5
Liquor group	3 = >148 cl		28/9	5.5	2.1–14

[1]The score for amount consumed on each occasion (1–4) was multiplied with frequency scores (1–4) to produce the total score values. ORs were calculated for total score values as well as for total consumption volume per month.–[2]Ca/Co = cases/controls.

TABLE V – ORs FOR ALL EXPOSURE FACTORS, UNIVARIATE AND MULTIVARIATE ANALYSES[1]

Exposure factor	Univariate analysis		Multivariate analysis	
	OR	95% CI	OR	95% CI
Snuff	0.9	0.6–1.4	0.8	0.5–1.3
Smoking	1.2	0.8–1.8	1.1	0.7–1.6
Light beer	1.4	1.0–2.0	1.2	0.7–1.7
Beer	1.9	0.9–3.9	1.5	0.7–3.2
Wine	1.3	0.9–1.8	1.0	0.6–1.5
Liquor	1.6	1.1–2.3	1.5	0.9–2.3

[1]Only subjects with data available for all factors are included.

were beer and liquor consumption followed by smoking (Table V). However, no OR was statistically significant.

To further evaluate if there existed any important interaction between the 3 factors—smoking, oral snuff and alcohol consumption—pairwise analyses were done and results are presented in Tables VI and VII. Smoking tobacco appeared to be a risk factor independent of oral snuff use. For oral snuff use and liquor consumption, the risk decreased with the dose of oral snuff in the group high consumption of alcohol, a tendency not seen in the other alcohol consumption groups (Table VI). Smoking tobacco and liquor appeared to interact with the highest risk in the highest consumption group of both exposures.

DISCUSSION

Our primary aim was to investigate the role of moist snuff in the etiology of oral cancer. The use of this form of tobacco is a widespread and increasing habit in Sweden (Andersson, 1991; Pershagen, 1996), and has been much discussed in recent years.

We also considered it important to investigate the role of the established risk factors of smoking and alcohol, since the incidence of oral cancer is increasing in Sweden, traditionally a low incidence area (Boyle *et al.*, 1995). This trend is especially notable in light of a decrease in smoking habits among men, parallel to the increase in snuff use (Anonymous, 1986; Ramström, 1989).

Thanks to population registries and the national cancer registration in Sweden, this country is particularly suitable for population-based case-control studies. The cases were recruited from the Regional Cancer Registry of Northern Sweden. The Swedish compulsory reporting system for malignant diseases makes it most likely that practically all incident cases in the study base were included.

In Sweden, complete population registries cover the whole population, which permits the use of a control group from the general population, thereby avoiding selection bias. Efficacy in the analyses was increased by using a matched study design controlling for age, sex, county and vital status. The reason for using dead controls is the matter of comparability in data collection between cases and controls, *i.e.*, to obtain similar recall conditions.

In case-control studies, there is always a possibility of recall bias, *e.g.*, a tendency for the cases to remember or express more hazardous exposures than controls. To further reduce this risk, the aim of the study was concealed. Thus, no allusion to the disease under study was made in information given to the subjects. Furthermore, the questionnaire asked for information on many different occupational and other exposure factors, not only tobacco and alcohol habits. Results of other factors of interest will be analyzed and published later.

Oral snuff was not found to be a risk factor for oral cancer in our study. Former snuff users showed a tendency to increased risk, compared with current snuff users who rather had a decreased risk. The reason for this paradoxical finding, also noted by Lewin *et al.* (1998), is unclear but one possibility could be that persons with mucosal problems and perhaps premalignant changes experienced inconvenience while using snuff, and therefore stopped this habit, and thereby constituted a group with a potentially increased risk for oral cancer. The suggested hypothesis that ex-snuff users tend to be current smokers was considered. However, in the presented material, only 1 person had begun smoking after having quit using snuff.

Our finding of a slight but not significantly increased risk for cancer of the lip in users of oral snuff might be in accordance with other findings describing a local mucosal reaction caused by the use of snuff. Studies on the histopathology of mucosal reaction have been carried out in the United States (Smith *et al.*, 1970), Denmark (Roed-Peterson and Pindborg, 1973) and Sweden (Andersson *et al.*, 1989; Axell *et al.*, 1976) whereby epithelial changes have been described, but in most cases, such changes were seen in the outermost layers of the mucosa only. Axell *et al.* (1976), in the material of 114 biopsies from current snuff dippers in Sweden, found no cellular atypia or epithelial dysplasia. Andersson *et al.* (1989) did not find any epithelial dysplasia in biopsies from 252 current Swedish snuff users either.

The manufacturing processes for Swedish and American snuff differ and result in different concentrations of tobacco-specific N-nitrosamines (TSNA). When analyzing nitrosamines in both types of snuff, much higher concentrations were found in American snuff (up to 18-fold higher) compared with Swedish snuff (IARC,

TABLE VI – ORs FOR ORAL CANCER DEPENDENT ON LIFE CONSUMPTION OF ORAL SNUFF, SMOKING TOBACCO AND LIQUOR USE

	Liquor[1]											
	Never liquor			Low consumption			Medium consumption			High consumption		
	Ca/Co[2]	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Oral snuff[3]												
Never snuff	99/125	1.0		88/92	1.4	0.9–2.1	44/34	2.1	1.1–3.8	33/8	7.4	2.8–20
Low consumption	5/9	1.2	0.3–4.2	6/11	0.7	0.2–2.1	6/4	2.8	0.7–11	5/3	2.7	0.5–13
High consumption	2/2	1.8	0.2–16	17/11	2.6	1.0–6.4	6/9	1.1	0.3–3.7	1/4	0.4	0.0–3.5
Smoking tobacco[4]												
Never smokers	80/100	1.0		50/45	1.2	0.8–1.9	7/11	1.4	0.8–2.6	4/2	4.2	1.8–9.4
Low consumption	15/22	1.0	0.6–1.6	26/31	1.2	0.6–2.1	19/17	1.4	0.7–2.7	4/4	4.0	1.6–9.8
High consumption	8/9	1.4	0.8–2.3	30/31	1.6	0.9–2.9	27/21	2.0	1.0–3.6	30/7	5.7	2.4–14

[1]Liquor consumption. Low: score 1–3; medium: score 4–8; high: score 9–16.–[2]Ca/Co = cases/controls.–[3]Life consumption of oral snuff. Low: life consumption ≤156.0 kg; high: life consumption >156.0 kg.–[4]Life consumption of smoking tobacco. Low: life consumption ≤124.8 kg; high: life consumption >124.8 kg.

TABLE VII – ORs FOR ORAL CANCER DEPENDENT ON LIFE CONSUMPTION OF SMOKING TOBACCO AND ORAL SNUFF

Smoking tobacco[1]	Oral snuff[2]								
	Never snuff			Low consumption			High consumption		
	Ca/Co[3]	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Never smokers	117/133	1.0		4/8	0.8	0.4–1.6	13/12	1.3	0.6–2.6
Low consumption	48/52	1.2	0.7–1.9	6/7	1.0	0.4–2.1	7/7	1.5	0.6–3.5
High consumption	79/58	1.8	1.1–2.9	10/8	1.5	0.6–3.3	3/2	2.3	0.9–5.6

[1]Life consumption of smoking tobacco. Low: life consumption ≤124.8 kg; high: life consumption >124.8 kg.–[2]Life consumption of oral snuff. Low: life consumption ≤156.0 kg; high: life consumption >156.0 kg.–[3]Ca/Co = cases/controls.

1985). This difference, as well as the 1.5–2-fold higher concentrations of nicotine in American snuff (Djordjevic *et al.*, 1993), may be one explanation why our results differ from American ones on the cancer risk from oral snuff use.

Other forms of locally adapted tobacco have been associated with an increased risk of oral cancer. Thus, in India the chewing of the betel quid, with or without tobacco, is a very widespread habit. The basic betel quid consists of betel leaf, arcea nut and lime. Chewing these quids is associated with oral cancer (IARC, 1985). However, these quids differ considerably from Swedish moist snuff, and conclusions drawn from one may not be at all valid for the other.

Our results confirm the earlier findings of smoking and alcohol as risk factors for oral cancer. However, the rather low risk from smoking, as well as the lack of any risk in ex-smokers, are not in accordance with some other studies from Europe. The proportion of current smokers among the cases and controls is, indeed, consistent with Swedish smoking statistics (National Board of Health and Welfare, 1986; Pellmer and Wramner, 1997). Studies from, *e.g.*, Italy, generally show much higher ORs compared with our results (Franceschi *et al.*, 1992). One could speculate that the difference lies in different drinking and smoking habits, different types of cigarettes and perhaps even genetic differences.

The majority of subjects in our study had deceased and the exposure information from relatives could potentially have been inaccurate. Furthermore, the use of deceased controls is a theoretical problem when studying factors such as tobacco and alcohol drinking, which are related to earlier death. For these reasons, we also analyzed the main potential risk factors separately for alive subjects only, *i.e.*, when exposure information was given by the living subjects themselves. This did not lead to significantly different ORs for tobacco exposure, compared to the overall results, but lower ORs were found for alive subjects admitting liquor consumption, indicating recall bias for this group.

In this study, there was no increased risk for ex-smokers for this type of malignancy. This result is in contrast with the findings of a study from Florida, where elevated risks also for ex-smokers were noted (Stockwell and Lyman, 1986). In that study, alcohol data were not known, however, and the data must be interpreted with caution, since alcohol might be an important confounder. In other studies, however, no significantly increased risks among ex-smokers were found (Blot *et al.*, 1988; Mashberg *et al.*, 1993).

Tumors located in the floor of the mouth showed the strongest correlation with smoking in our study. This confirms results from previous studies (*e.g.*, Stockwell and Lyman, 1986).

In our study, cigarette smoking totally dominated the types of smoking habits followed by pipe smoking. The use of cigars and cheroots was too infrequent to permit an evaluation of any association with oral cancer.

Alcoholic beverages turned out to be the strongest risk factor for oral cancer in our study. As in some other studies, (Bundgaard *et al.*, 1995; Blot *et al.*, 1988; Mashberg *et al.*, 1993), the increased risk was confined to beer and liquor, whereas wine drinking only appeared to constitute a risk factor for high consumers as in Italy (Franceschi *et al.*, 1992). The dose-response effect regarding liquor strongly supports this finding.

Tobacco and alcohol may be expected to occur together among many consumers. To investigate the relative importance of each factor a multivariate analysis was performed. Liquor turned out to be the strongest associated factor, followed by beer and light beer, although the ORs did not differ significantly. The differences in the detection of statistically significant differences among the ORs between the multivariate and univariate analyses may be attributable to sample size and intercorrelations between variables.

In conclusion, our results do not support any association between the use of oral snuff and oral cancer. Current smoking was correlated with this disease, but to a lesser extent than in some other studies, mainly from countries with a higher incidence of the disease. For alcohol, our results support earlier findings on beer and liquor as being rather strong risk factors for oral cancer.

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